

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 10/518,814 Confirmation No. : 8244
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Inventor
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TC/A.U. : 1617
Examiner : Sahar Javanmard

Docket No. : 101512.55677US
Customer No. : 23911
Title : Method of Photodynamic Diagnosis for Vascular Diseases

REPLY BRIEF

Mail Stop Appeal Brief- Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Examiner's Answer dated July 22, 2009, this Reply Brief is filed pursuant to 37 C.F.R. § 41.41.

I. STATUS OF CLAIMS

The status of claims, which is reproduced here, is as set forth on page 2 of the Appeal Brief filed March 26, 2009.

Claims 1-2, 7-8, and 13-14 are currently pending in this application. All of these claims stand rejected, and all of these rejections are being appealed. Accordingly, the following is a statement of the status of all claims in this proceeding:

- Claim 1. Rejected, and being appealed.
- Claim 2. Rejected, and being appealed.
- Claim 3. Cancelled.
- Claim 4. Cancelled.
- Claim 5. Cancelled.
- Claim 6. Cancelled.
- Claim 7. Rejected, and being appealed.
- Claim 8. Rejected, and being appealed.
- Claim 9. Cancelled.
- Claim 10. Cancelled.
- Claim 11. Cancelled.
- Claim 12. Cancelled.
- Claim 13. Rejected, and being appealed.
- Claim 14. Rejected, and being appealed.
- Claim 15. Cancelled.
- Claim 16. Cancelled.
- Claim 17. Cancelled.
- Claim 18. Cancelled.

Claims 3-6, 9-12, and 15-18 were previously canceled and are not being appealed. Appellants hereby seeks reversal of the final rejection of claims 1-2, 7-8, and 13-14.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be review on appeal, which are reproduced here, are as set forth on page 5 of the Appeal Brief filed March 26, 2009. These grounds are:

- (i) whether claims 13 and 14 are obvious under 35 U.S.C. § 103(a) over Hikida et al., (US 6,063,777); and
- (ii) whether claims 1-2 and 7-8 are obvious under 35 U.S.C. § 103(a) over Hikida et al. in view of Levy (Trends Biotechnology, 1995).

III. ARGUMENT

A. *Claims 13 and 14 Are Not Obvious Over Hikida et al. Under 35 U.S.C. § 103(a).*

The present inventors have discovered an improved method for locating the sentinel lymph node and the presence of cancer metastasis. As presently claimed in independent claim 13, this method comprises administering an iminochlorine aspartic acid derivative of formula (I) or a pharmaceutically acceptable salt thereof and detecting fluorescence with a fluorescent imaging system. As apparent from the specification, the fluorescence is emitted by the iminochlorine aspartic acid derivative of formula (I) or a pharmaceutically acceptable salt thereof present in the sentinel lymph node. Thus, it is necessary for the compound to accumulate and remain in the sentinel lymph node so that fluorescence emitted by the compound present in the sentinel lymph node may be detected with a fluorescent imaging system. See page 16, line 28-page 18, line 16 of the specification.

Page 9 of the Examiner's Answer alleges that it would be obvious to try to use the compound of Hikida et al. to locate the sentinel lymph node because the compound of Hikida et al. is useful for diagnosis and treatment of cancer.

On the contrary, it would not be obvious to try to use the compound of Hikida et al. to determine the location of a sentinel lymph node and, subsequently, the presence of cancer metastasis. Hikida et al. does not disclose or suggest that its compound accumulates in lymph nodes, and certainly does not disclose or suggest that its compound accumulates in the sentinel lymph node. Hikida et al. discloses that its compound accumulates in some cells more than others. The compound selectively accumulates in tumor cells and is excreted therefrom at a slow rate, while excretion from normal organs and cells is rapid. Col. 7, lines 16-20. In particular, the compound accumulates in exogenously added tumor cells. See Example 8. Furthermore, as evident from Hikida et al., distribution of the compound varies among different organs and cells including lung, muscle, brain, liver, and kidney. See Table 1 at col. 10, lines 15-25. However, there is no indication or suggestion in Hikida et al. that its compound preferentially accumulates in any lymph nodes, including the sentinel lymph node.

Furthermore, it would not be obvious to try to use the compound of Hikida et al. in the presently claimed method because Hikida et al. **does not** disclose or suggest **how** to diagnose cancer with its compound. Hikida et al. generally discloses that its compound can be used for the diagnosis or treatment of cancer. However, Hikida et al. does not describe or suggest **how** one of ordinary skill in the art **would actually use its compound to diagnose**

cancer. Hikida et al. only demonstrates that its compound eliminates more slowly from exogenously added tumor cells. Hikida et al. does not demonstrate that its compound eliminates more slowly from endogenously produced tumor cells.

Additionally, the Examiner's present application of "obvious to try" falls within the two classes of improper obvious to try rationales. In *In re Kubin*, 561 F.3d 1351, 90 USPQ2d 1417 (Fed. Cir. 2009), the Federal Circuit reminded the Office, patent practitioners, and inventors of two classes of improper obvious to try rationales. One of these improper obvious to try rationales occurs when "what was 'obvious to try' was to explore a new technology or general approach that seemed to be a ***promising field of experimentation***, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." 561 F.3d at 1359, 90 USPQ2d at 1423 (quoting *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988))(emphasis added). The second improper obvious to try rationale discussed in *In re Kubin* is "what would have been 'obvious to try' would have been to vary all parameters or ***try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.***" 561 F.3d at 1359, 90 USPQ2d at 1423 (quoting *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1998))(emphasis added).

The Examiner has applied the first class of improper obvious to try rationale, i.e., "promising field of experimentation." Hikida et al.'s disclosure is no more than a disclosure that ***diagnosing and treating cancer with its compound is a promising field of experimentation.*** At best, Hikida et al. shows that diagnosing and treating cancer with its compound in ***organs other than lymph nodes, including lung, muscle, brain, liver, and kidney,*** is a promising field of experimentation. But Hikida et al. certainly does ***not*** disclose or suggest that diagnosing and treating cancer with its compound in ***lymph nodes*** is a promising field of experimentation.

The Examiner's obvious to try rationale is also an improper application of the second class of improper obvious to try rationale, i.e., "trying each of numerous possible choices until one possibly arrives at a successful result, where the prior art gives no direction as to which of many possible choices is likely to be successful." Cancer can grow in and spread to ***numerous organs*** in the body. In order to arrive at the presently claimed methods, one of

ordinary skill in the art would have had to experiment with *all photosensitizers* of which Hikida et al.'s photosensitizer is just one, and also determine accumulation and retention of the photosensitizers in the numerous different organs in the body. However, Hikida et al. does not give any indication that Hikida's *particular photosensitizer* will be successful in locating *any lymph nodes, including the sentinel lymph node, from among the various organs* in the body. At best, Hikida et al. directs one of ordinary skill in the art to locate cancer in organs *other than lymph nodes, including lung, muscle, brain, liver, and kidney*.

Moreover, there is no requisite teaching, suggestion, or motivation and reasonable expectation of success in using the compound of Hikida et al. to determine the location of a sentinel lymph node and, subsequently, the presence of cancer metastasis. A *prima facie* case of obviousness requires some teaching, suggestion, or motivation to combine elements of the prior art in the prior art itself, the nature of the problem, or the knowledge of a person with ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct., 1727, 1734, 82 USPQ 2d 1385, 1391 (2007). A *prima facie* case of obviousness also requires a reasonable expectation of success in modifying or combining the elements of the prior art to arrive at the claimed invention. M.P.E.P. § 2143.02. The Office apparently alleges that the usefulness of the compound of Hikida et al. for the diagnosis and treatment of cancer provides the requisite teaching, suggestion, or motivation and reasonable expectation of success to modify Hikida et al. to arrive at the presently claimed method. See Examiner's Answer at page 6 and Advisory Action mailed December 23, 2008 at page 2. However, Hikida et al.'s disclosure that its compound is useful for diagnosis and treatment of cancer based on the differential retention of the compound in exogenously added tumor cells versus a select subset of normal organ cells, as set forth in Example 8, does not provide any teaching, suggestion, or motivation and reasonable expectation of success to locate the *sentinel lymph node*. Hikida et al.'s disclosure that its compound selectively accumulates in *cancer cells* does *not* translate to a teaching, suggestion, or motivation and a reasonable expectation of success that Hikida et al.'s compound would also accumulate in *lymph nodes, including the sentinel lymph node*.

The arguments set forth in the Appeal Brief filed March 26, 2009 regarding the obviousness rejection of claims 13-14 continue to apply and are incorporated herein by reference.

Accordingly, for at least the reasons discussed above and the reasons set forth in the Appeal Brief filed March 26, 2009, the Board's reversal of the obviousness rejection of claims 13-14 is respectfully requested.

B. *Claims 1, 2, 7, and 8 Are Not Obvious Under 35 U.S.C. § 103(a) Over Hikida et al. in view of Levy.*

The present inventors have also discovered a new method for treating rheumatoid arthritis by photodynamic therapy. Additionally, the present inventors have discovered a new method for treating inflammatory keratosis by photodynamic therapy. These new methods are claimed in independent claims 1 and 7 and both comprise administering an iminochlorine aspartic acid derivative of formula (I) or a pharmaceutically acceptable salt thereof.

Page 11 of the Examiner's Answer alleges that it would be obvious to try to use the compound of Hikida et al. to treat both rheumatoid arthritis and inflammatory keratosis in view of Levy. The Examiner's allegation is an improper application of "obvious to try."

Levy merely discloses that *rheumatoid arthritis and psoriasis are promising fields of experimentation of photodynamic therapy*. As discussed above, exploring a promising field of experimentation is not an appropriate obvious to try rationale. As discussed in the Appeal Brief filed March 26, 2009, Levy discloses *potential* indications for photodynamic therapy, including rheumatoid arthritis and psoriasis, and discusses the *possibility* of photodynamic therapy for these diseases. See page 14, paragraph under heading "Clinical status of PHOTOFRIN®" and Table 1 of Levy. Thus, the Examiner's obvious to try rationale is inappropriate.

Furthermore, the Examiner's application of obvious to try to the presently claimed methods of treating rheumatoid arthritis and inflammatory keratosis by photodynamic therapy is improper because it requires one of ordinary skill in the art to throw "metaphorical darts at a board filled with combinatorial prior art possibilities." *In re Kubin*, 561 F.3d 1351, 1359, 90 USPQ2d 1417, 1423 (Fed. Cir. 2009). The dart board metaphor refers to the second improper obvious to try rationale discussed above, which involves varying all parameters or *trying each of numerous possible choices until one possibly arrived at a successful result, where the prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful*. In order to arrive at the presently claimed methods, one of ordinary skill in the art would have had to experiment with

the **general class of photosensitizer compounds** in the treatment of rheumatoid arthritis and psoriasis to arrive at the presently claimed methods. Neither Hikida et al. nor Levy give any indication that **Hikida et al.'s particular photosensitizer** would be successful in the treatment of rheumatoid arthritis or psoriasis. In fact, as discussed in Applicants' responses of February 26, 2008 and November 13, 2008, the photosensitizers disclosed in Levy are structurally different from the compound of Hikida et al. Thus, the structures of the photosensitizers of Levy do not provide any indication that Hikida et al.'s particular photosensitizer, out of the general class of photosensitizers, is likely to be successful for the treatment of rheumatoid arthritis or psoriasis. Rather, the structural differences militate against any indication of success.

Due to the structural differences between the compound of Hikida et al. and the compounds disclosed in Levy, there is no requisite teaching, suggestion, or motivation and reasonable expectation of success to employ the specific compound of Hikida et al. in photodynamic therapy to treat rheumatoid arthritis or psoriasis. It is well known in the art that compounds with differences in structure, even small differences in structure, generally have different properties. Accordingly, one of ordinary skill in the art would not reasonably think to choose the compound of Hikida et al. to treat the indications disclosed in Levy.

Thus, in the rejection of claims 1-2 and 7-8, the Examiner has merely attempted to abstract individual teachings from the different pieces of prior art to create the combination upon which the rejection of the present claims was based. This is an error as a matter of law. *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 1552, 220 USPQ 303, 312 (Fed. Cir. 1983).

The arguments set forth in the Appeal Brief filed March 26, 2009 regarding the obviousness rejection of claims 1-2 and 7-8 continue to apply and are incorporated herein by reference.

Accordingly, for at least the reasons discussed above and the reasons set forth in the Appeal Brief filed March 26, 2009, the Board's reversal of the obviousness rejection of claims 1-2 and 7-8 is respectfully requested.

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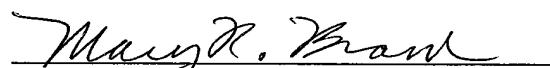
IV. CONCLUSION

In conclusion, Appellants submit that claims 1-2, 7-8, and 13-14 are patentable over the prior art of record for the reasons stated in their Appeal Brief and this Reply Brief.

Although no fees should be due in connection with this Reply Brief, the Director is authorized to charge any deficiency, or credit any overpayment, to Deposit Account no. 05-1323 (Docket No.: 101512.55677US).

Respectfully submitted,

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